Mitochondrial dysfunction in CA1 hippocampal neurons of the UBE3A deficient mouse model for Angelman syndrome.

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Public Summary:

Scientific Abstract:
Angelman syndrome (AS) is a severe neurological disorder caused by a deficiency of ubiquitin protein ligase E3A (UBE3A), but the pathophysiology of the disease remains unknown. We now report that in the brains of AS mice in which the maternal UBE3A allele is mutated (m-) and the paternal allele is potentially inactivated by imprinting (p+) (UBE3A m-\p+), the mitochondria are abnormal and exhibit a partial oxidative phosphorylation (OXPHOS) defect. Electron microscopy of the hippocampal region of the UBE3A m-\p+ mice (n=6) reveals small, dense mitochondria with altered cristae, relative to wild-type littermates (n=6) and reduced synaptic vesicle density. The specific activity of OXPHOS complex III is reduced in whole brain mitochondria in UBE3A m-\p+ (n=5) mice versus wild-type littermates (n=5). Therefore, mitochondrial dysfunction may contribute to the pathophysiology of Angelman syndrome.